

REMARKS

In the specification, the legend of Figure 2 in paragraph 22 beginning on page 9 of the substitute specification and the legend of Figure 3 in paragraph 24 beginning on page 10 of the substitute specification have been amended to comply with the Examiner's directive concerning trademarks. No new matter is added.

The Examiner has requested that relevant portions of disclosure in U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991 (which is incorporated by reference in the above-captioned application at paragraph 29 on page 12 of the substitute specification filed July 27, 2001) be added to the specification of the above-referenced application to provide written support for the elements of the limitations describing the polypeptides "malignin" and "Recognin-M." As such, in the specification, paragraphs 33 to 43 (and headings for the examples contained therein) are added following paragraph 32 on page 14 of the substitute specification. The added text is either taken directly from, or in a few transitional phrases derived from, the specification of U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991. No new matter is added.

The heading before paragraph 33 is taken from lines 10-12 on page 31 of the specification of U.S. Appln. Ser. No. 07/744,649 as filed. Example 5 is renumbered to Example 12 to conform to the progression of examples in the above-captioned application. Paragraph 33 is taken from lines 13 and 14 of page 31 of U.S. Appln. Ser. No. 07/744,649 and from Examples 3 and 4 of U.S. Appln. Ser. No. 07/744,649 wherein preparation of the crude malignin-containing fraction is described. Paragraph 34 is taken from line 21 on page 22 through line 20 on page 25 of U.S. Appln. Ser. No. 07/744,649. In paragraph 34, references to Astrocytin are changed to references to Malignin as described at lines 13 and 14 on page 31 of U.S. Appln. Ser. No. 07/744,649. Paragraphs 35-38 are taken from line 15 on page 31 through the end of page 32 of U.S. Appln. Ser. No. 07/744,649. Paragraph 39 is derived from column 2 of Table III on page 38 of U.S. Appln. Ser. No. 07/744,649.

The heading before paragraph 40 is taken from lines 28 and 29 on page 34 of U.S. Appln. Ser. No. 07/744,649. The Example is renumbered from 5B to 13 to conform to the progression of examples in the above-captioned application. Paragraphs 40-42 are taken from line 30 on page 34 through line 19 on page 36 of U.S. Appln. Ser. No. 07/744,649. Paragraph 43 is derived from column 3 of Table III on page 38 of U.S. Appln. Ser. No. 07/744,649.

Amendments to the specification are made based on the substitute specification filed July 27, 2001, a copy of which was resubmitted with a statement of no new matter in the response filed August 15, 2005.

Claims 1 to 4 and 14 are pending. Claims 5 through 13 are canceled. Claims 1 and 14 are amended in response to the objections to the claims in the final Office Action mailed November 19, 2008 and to conform the claim language to the thin layer chromatographic conditions disclosed in U.S. Appln. Ser. No. 07/744,649 on page 22 of the specification (which conditions have now been added to the specification of the above-captioned application as paragraph 34). No new matter is added.

Applicant reserves the right to pursue the canceled claims and the subject matter of the original claims in a continuation application.

Support for the amendment to claim 1 may be found, for example, at lines 23-25 on page 22, lines 5-7 on page 29, and line 25 on page 32 of U.S. Appln. Ser. No. 07/744,649, which is incorporated by reference in the above-captioned application at paragraph 29 on page 12 of the substitute specification filed July 27, 2001. Further support may be found, for example, in Examples 2-5 of U.S. Appln. Ser. No. 07/744,649.

Support for the amendment to claim 14 may be found, for example, at lines 23-25 on page 22 and line 30, page 34 through line 6, page 35 of U.S. Appln. Ser. No. 07/744,649, which is incorporated by reference in the above-captioned application at paragraph 29 on page 12 of the substitute specification filed July 27, 2001. Further support may be found, for example, in Example 5B of U.S. Appln. Ser. No. 07/744,649. Additional support may also be found in Examples 1-5 of U.S. Appln. Ser. No. 07/744,649.

Non-Compliant Amendment under 37 C.F.R. § 1.121

The Examiner asserts that the amendment filed July 14, 2008 is non-compliant because it directs the replacement of paragraphs in the specification of the application as filed May 15, 2001 rather than in the substitute specification filed July 27, 2001. In the present response, amendments to the specification are directed to the substitute specification filed July 27, 2001 (a copy of which was submitted with the response filed August 15, 2005) and the amendments to the specification in the response filed July 14, 2008 are resubmitted. The Applicant respectfully requests withdrawal of this objection.

The Applicant respectfully notes that the Examiner appears to have mistakenly referenced an amendment filed November 15, 2006 when the Examiner discussed the non-compliant amendment under 37 C.F.R. § 1.121 in item 3 on page 2 of the Office Action mailed November 19, 2008. It is the Applicant's understanding that the Examiner actually meant to reference the amendment filed July 14, 2008, as discussed above. The Applicant has this understanding because there is no amendment filed November 15, 2006 in the above-captioned application and because the Examiner's comments appear to correspond with the amendment filed July 14, 2008. As such, the Applicant understands that the above-discussed amendments to the specification are a proper response to the Examiner's request for resubmission of the amendments to the specification.

Priority Benefit under 35 U.S.C. § 120

The Examiner finds claims 1-4 and 14 do not properly benefit under 35 U.S.C. § 120 from an earlier claimed filing date because the claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure. As set forth above and discussed below, the Applicant has amended claims 1 and 14 (based on the Examiner's rejection of the claims for lack of written description and enablement) to be directed to a polypeptide isolated from, respectively, "glioma cancer cells" or "MCF-7 cells." The Applicant respectfully submits that this amendment responds to the Examiner's rejection of claims 1 and 14 for lack of written description and enablement. The Applicant further submits that claims 2-4, which depend from independent claim 1, also overcome the Examiner's rejection in view of the amendment of claim 1.

Because the amendment to claims 1 and 14 respond to the rejection of the claims for lack of written description and enablement, the Applicant respectfully requests the Examiner withdraw the finding that claims 1-4 and 14 do not benefit under 35 U.S.C. § 120 from the earliest filing date of August 8, 1991.

The Examiner further appears to find that the first paragraph of the specification claims priority to U.S. Appln. Ser. No. 04/385,451, filed August 3, 1973. The Applicant disagrees and finds that the first paragraph of the specification as amended by the Amendment and Response of August 15, 2005 claims priority to U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991.

The Applicant respectfully believes the Examiner is mistaken in finding the application claims priority to U.S. Appln. Ser. No. 04/385,451, filed August 3, 1973. The Applicant respectfully believes the Examiner is mistaken because the Examiner mistakenly considers the copy of the July 27, 2001 substitute specification submitted for the second time as a courtesy on August 15, 2005 to be an amendment to the specification as of August 15, 2005 rather than as a copy of the substitute specification filed on July 27, 2001. The Amendment and Response filed August 15, 2005 makes clear that the substitute specification enclosed therewith is simply a copy of the July 27, 2001 substitute specification. In the Amendment and Response filed August 15, 2005, the Applicant expressly states: "Applicant additionally requests entry of the Substitute Specification filed on July 27, 2001, a copy of which is enclosed herewith, and state under 37 C.F.R. § 1.125(b) that the Substitute Specification contains no new matter." Because the Applicant requested entry of the substitute specification filed July 27, 2001, the amendment to the first paragraph of the specification contained in the August 15, 2005 Amendment and Response should have been entered. In the final Office Action of February 13, 2006, the amendment to the first paragraph of the specification made in the Amendment and Response of August 15, 2005 was officially entered. As such, the Applicant respectfully submits the above-captioned application claims priority to U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991 and does not claim priority to U.S. Appln. Ser. No. 04/385,451, filed August 3, 1973.

The Applicant respectfully requests the Examiner acknowledge the application claim of priority to U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991 as set forth in the Amendment and Response of August 15, 2005 and as entered by the Office in the final Office Action of February 13, 2006.

The Examiner further asserts that claim 14 does not properly benefit from any filing dates prior to Appln. Ser. No. 06/019,078 because none of the earlier applications describe Recognin-M. Recognin-M is fully described in the presently-claimed priority document U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991. For example, Recognin-M is fully described in Example 5B and Table III at pages 34-38 of U.S. Appln. Ser. No. 07/744,649. As such, the Applicant respectfully requests the Examiner acknowledge the priority of claim 14 to U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991.

Improperly Demarcated Trademarks

The Examiner maintains the earlier objection to the specification for improperly demarcated trademarks. In the amendments to the specification contained herein, each letter of identified trademarks is capitalized in accordance with the request of the Examiner. As such, the Applicant respectfully requests withdrawal of the objection.

Antecedent Basis under MPEP § 608.01(o)

The Examiner objects to the specification as not providing antecedent basis for claims 1 and 14. As suggested by the Examiner, the Applicant has amended the specification to add written support for the elements describing the polypeptides “malignin” and “Recognin-M.” Paragraphs 33 to 43 (and headings for the examples contained therein) are added following paragraph 32 on page 14 of the substitute specification. The added text is either taken directly from, or in a few transitional phrases derived from, the specification of U.S. Appln. Ser. No. 07/744,649, filed August 8, 1991. No new matter is added. Because antecedent basis for claims 1 and 14 has been added to the specification of the above-captioned application from U.S. Appln. Ser. No. 07/744,649, the Applicant respectfully requests withdrawal of this objection.

Rejection of Claims 1-4 and 14 for Written Description

The Examiner has rejected claims 1-4 and 14 as failing to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. The Examiner asserts that claims 1-4 and 14 are too broad and should be directed to polypeptides “isolated from the same sources by the same processes described [in U.S. Appln. Ser. No. 07/744,649].” Office Action at 9. The Applicant has amended claim 1 to be directed to a polypeptide “isolated from glioma cancer cells” and characterized by the methods of U.S. Appln. Ser. No. 07/744,649. Likewise, the Applicants have amended claim 14 to be directed to a polypeptide “isolated from MCF-7 cells” and characterized by the methods of U.S. Appln. Ser. No. 07/744,649. The amendment to independent claim 1 should also overcome the rejection of dependent claims 2-4.

Because the Applicant has amended claims 1-4 and 14 as directed by the Examiner, the Applicant respectfully requests withdrawal of the rejection of the claims for lack of written description.

Rejection of Claims 1-4 and 14 for Enablement

The Examiner has rejected claims 1-4 and 14 as failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. The Examiner asserts that claims 1-4 must be directed to a malignin polypeptide that is isolated from glioma tumor tissue, namely, glioma cells. Office Action at 12. The Examiner further asserts that claim 14 must be directed to a Recognin-M polypeptide isolated from MCF-7 cells. Office Action at 13. The Applicant has amended independent claims 1 and 14 to be directed to a polypeptide isolated from “glioma cancer cells” and “MCF-7 cells,” respectively. Because claims 2-4 depend from claim 1, they are likewise amended to be directed to a polypeptide isolated from “glioma cancer cells.”

The Applicant respectfully requests withdrawal of the enablement rejection in view of the Applicant’s amendment of the claims based on the Examiner’s directions.

Obviousness Rejection of Claims 1-4

The Examiner rejects claims 1-4 as obvious over Bogoch *et al.*, Protides of Biological Fluids 31,739-747 (1984) and Bogoch *et al.*, Prog. Clin. Biol. Res. 1980; **39**: 407-424. The Examiner asserts that Bogoch *et al.* (1980) and Bogoch *et al.* (1984) when combined make it obvious to therapeutically administer malignin to a subject to produce and release anti-malignin antibody into the subject serum because both papers suggest that doing so “will be clinically effective against cancer.” Office Action at 16, second line from bottom and at 17 last sentence of second to last paragraph.

The Applicant respectfully and strongly disagrees. Bogoch *et al.* (1984) expressly state the opposite of the Examiner’s assertions concerning obviousness. The papers, in fact, teach away from the claimed invention and expressly demonstrate that one of ordinary skill in the art would not have been led to modify the prior art to overcome the differences between the scope and contents of the prior art and the claimed invention with any reasonable level of predictability. See MPEP §§ 2141.03 and 2143(G).

For example, Bogoch *et al.* (1984) expressly state: “[I]t does not necessarily follow that because an antibody in situ is shown to be related to survival that replacement or increase of the concentration of that antibody by means of either the classical methods of active or passive immunotherapy will be clinically effective against cancer.” *Id.* at 746 third sentence, second to last paragraph (emphasis added). Furthermore, Bogoch *et al.* (1980) make clear that its

teachings provide only a “potential therapeutic interest” to the skilled reader requiring further testing. *Id.* at 422 last sentence of third paragraph (emphasis added) and 423.

Both papers teach away from a finding that a cancer therapy is the obvious conclusion of the cited art in combination. For example, Bogoch *et al.* (1980) teach that “the use of [malignin] to stimulate antibody production in the patient will . . . be tested.” *Id.* at 423 (emphasis added). Bogoch *et al.* (1984) teach that the data supplied therein “make it . . . possible to investigate further [the] therapeutic activity and mechanism of action.” Bogoch *et al.* (1984) at 746 (emphasis added). Taken together, these teachings make abundantly clear to one of ordinary skill in the art that, as of the date of the cited art, the use of malignin in a cancer therapy was not reasonably predictable and had no reasonable expectation of success. MPEP §§ 2143.02 and 2143.03 (III). Instead, the papers make clear that further research is needed before effectiveness becomes predictable.

The further research that is expressly desired by the artisan in the cited prior art is explicitly provided in the above-captioned application. For example, the above-captioned application teaches that anti-malignin antibody is inhibitory to malignant cells in a concentration of picogram per cell. *See* Appln. ¶¶ 21-22 on page 9 of the substitute specification. The above-caption application further teaches that anti-malignin antibody increases in concentration in normal human serum with age and decreases in the serum of cancer patients after successful treatment resulting in no evidence of clinical cancer. *See* Appln. ¶¶ 23-25 on page 10 of the substitute specification. These combined data, among others, were not disclosed in Bogoch *et al.* (1980) or Bogoch *et al.* (1984).

Nonetheless, the above-captioned application teaches that these data provide support for an expectation of success of one of ordinary skill in the art because, among other things, (1) the exceedingly high cytotoxicity of the malignin antibody (at picograms per cell) provides the ordinary skilled artisan with an expectation that malignant cells will be inhibited if exposed to even a clinically minimal amount of increased anti-malignin antibody (Appln. ¶ 12 on pages 3-4 of substitute specification) and (2) maturation of anti-malignin antibody with human age provides evidence that the antibody is, in fact, produced in response to increased transformation of normal cells to malignant cells, *i.e.*, in combination with other data, a direct inhibitory response to cell transformation (Appln. ¶ 25 on pages 10-11 of substitute specification). Absent

such data demonstrating the effectiveness of anti-malignin antibody in inhibiting glioma cells in a patient, the ordinary skilled artisan would not possess a reasonable expectation of success. Bogoch *et al.* (1980) and Bogoch *et al.* (1984) both expressly make this assertion when each papers teaches the skilled artisan that further research is necessary and when Bogoch *et al.* (1984) expressly state: “[I]t does not necessarily follow that because an antibody in situ is shown to be related to survival that replacement or increase of the concentration of that antibody . . . will be clinically effective against cancer.” *Id.* at 746 third sentence, second to last paragraph (emphasis added).

In view of the teachings of the cited prior art, the Applicant respectfully asserts that Bogoch *et al.* (1980) and Bogoch *et al.* (1984) do not render claims 1-4 obvious but, instead, make clear that claims 1-4 were nonobvious as of the dates of those papers. Because both pieces of cited art teach away from a conclusion that the subject matter of claims 1-4 is reasonably predictable and obvious to one of ordinary skill in the art, the Applicant respectfully requests withdrawal of the rejection.

Rejection of Claims 1-4 and 14 for Indefiniteness

The Examiner rejects claims 1-4 and 14 for indefiniteness because of the term “Sephadex.” The Applicant has amended claims 1 and 14 to capitalize all letters in the term “SEPHADEX.” The Applicant respectfully submits that the amendment responds to the indefiniteness rejection. The Applicant makes this respectful submission for two reasons: First, MPEP 608.01(v) teaches that “[U]se of trademarks having definite meanings is permissible in patent applications [so long as] the proprietary nature of the marks [are] respected [by] capitalizing each letter of the mark” Second, a review of claims issued by the Patent Office from 1976 to the present reveals 221 patents having the term “Sephadex” in the claims, which demonstrates the Office’s conclusion that the term “Sephadex” has a definite meaning appropriate for issued patent claims.

Concerning the first reason, the Applicant respectfully submits that the most definite description of the thin layer chromatographic process described in the application employs the term “superfine Sephadex G-200.” One of ordinary skill in the art would immediately understand the meaning of this term. Any other description would be far less precise since the exact chromatographic characteristics of superfine Sephadex G-200 are apparently not easily

accessible to one of ordinary skill in the art. Further, the art of chromatography fully relies on the manufacturer to maintain exacting specifications for Sephadex G-200 over time. Any change in the specification would render an extensive body of scientific literature moot to further researchers because investigations described in the literature would not be repeatable. One of ordinary skill in the art has every expectation that “superfine Sephadex G-200” is a trademark which does not “arbitrarily” define the product and is not “liable to mean different things at the pleasure of manufacturers.” MPEP 608.01(v)(I). As such, the Applicant respectfully submits that the term “Sephadex G-200” is permissible because it is a trademark having a “definite meaning.” *Id.*

The Applicant further submits the Office has generally arrived at the same conclusion concerning the term “Sephadex” in other applications. For example, a review of issued patents from 1976 to the present revealed 221 patents having the term “Sephadex” in the claims. The latest patent having such a claim appears to have issued on October 7, 2008. Furthermore, a review of issued patents from 1976 to the present reveals 12 patents having the term “Sephadex G-200.”

Because the term “Sephadex G-200” has a definite and certain identity which is not expected to change over time and because the term “Sephadex” is extensively found in the claims of issued patents through the fall of 2008, the Applicant respectfully requests the Examiner withdraw this objection.

Rejection of Claim 14 for New Matter

The Examiner rejects claim 14 for new matter because “it does not appear that Application 07/744,649 describes a ‘Recognin-M’ polypeptide having a molecular weight of ‘approximately 10,000 Daltons.’” The Examiner further asserts that there is no disclosure in Application 07/744,649 describing the polypeptide eluting from a Sephadex G-50 resin column at approximately 0.9 with reference to Cytochrome C.

The Applicant respectfully submits that a Recognin-M of approximately 10,000 Daltons is described in U.S. Appln. Ser. No. 07/744,649. Such a disclosure may be found at the bottom of column 3 of Table III on page 38 of the specification as filed wherein Recognin M is disclosed as having a calculated molecular weight of 9,870 Daltons. On page 41 of the specification, the Applicant surmises that a lower apparent molecular weight of around 8,000 Daltons determined

using thin layer chromatography may be a function of a slightly lower net acidic charge on Recognin-M as compared to Malignin. Nonetheless, the calculation based on the amino acid constituency of the polypeptide is clearly “approximately 10,000 Daltons.” *See* page 38.

The Applicant further respectfully submits that the thin layer chromatographic process of now-amended claim 14 is disclosed in U.S. Appln. Ser. No. 07/744,649. For example, the process of the claims is expressly disclosed at lines 23-25 on page 22 and at line 30, page 34 through line 6, page 35 of U.S. Appln. Ser. No. 07/744,649. Further, the specification expressly states that the “molecular weight, amino acid composition, [and] behavior on thin layer gel chromatography . . . of [Recognin-M] is similar to those of . . . Malignin” As such, one of skill in the art would understand that the thin layer process disclosed on pages 22 and 31 of the specification for Malignin also applies to Recognin-M. Based on this disclosure, one of ordinary skill would understand from the data in Table III on page 38 that the Recognin-M polypeptide would elute at approximately 0.9 as compared to cytochrome C.

Because Recognin-M is disclosed in the specification of U.S. Appln. Ser. No. 07/744,649 as having a molecular weight of about 10,000 Daltons and because the process by which Recognin-M is characterized using thin layer chromatography is also disclosed in the specification of U.S. Appln. Ser. No. 07/744,649, the Applicant respectfully requests the Examiner withdraw the rejection of claim 14 as new matter.

CONCLUSION

It is believed that the present claims are in condition for allowance and Applicant earnestly requests the same. An early and favorable action on the merits is earnestly solicited.

The Examiner is invited to contact the undersigned agent to expedite allowance. The Commissioner is authorized to charged any fees or overpayments associated with this application to Kenyon & Kenyon LLP **Deposit Account No. 11-0600**.

Respectfully submitted,

KENYON & KENYON LLP

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